REMARKS

Claims 7, 8, 11, 16, 18, 19, 22 and 23 are currently amended. Claims 1-6, 14, 15, 25 and 26 were previously canceled without disclaimer or prejudice. Claims 7-13, 16-24 and 27-41 remain before the Examiner for reconsideration.

In the Office Action dated September 29, 2004, the Examiner objected to claims 8, 22, and 28-30, asserting the following informalities:

> In claim 8, line 2, "least" is misspelled. On line 4, "the imaging energy" lacks antecedent basis. Claim 22 is incomplete in that the claim fails to positively set forth a step of detecting extravasation as set forth in the preamble. Appropriate correction is required.

Applicants have amended claims 8 and 22 to obviate the Examiner's objections

The Examiner also rejected Claims 7, 8, 18, 33-34, 37 and 38 under 35 U.S.C. 102(b) "as being anticipated by Uber III et al ('026). Specifically, the Examiner asserted that: "Uber III et al disclose a first energy source 144 and a first sensor to measure a signal. The signal will inherently be proportional to the energy transformed, reflected, scattered, or absorbed by a fluid present in the vicinity of the site." Applicants respectfully traverse the Examiner's rejection.

To assert anticipation under Section 102(b) the cases hold that the Examiner:

> must show that each element of the claim in issue is found, either expressly described or under principles on inherency, in a single prior art reference, or, that the claimed invention was previously known or embodied in a single prior art device or practice.

Kalman v. Kimberly-Clark Corp., 713 F.2d 760, 771, 218 USPQ 781, 789 (Fed. Cir. 1983), cert. Denied, 465 U.S. 1026 (1984); Tyler Refrigeration v. Kysor Industrial Corp., 777 F.2d 687, 689, 227 USPQ 845, 846-47 (Fed. Cir. 1984) (judgment of anticipation reversed). "In deciding the issue of anticipation, the trier of fact must identify the elements of the claims, determine their meaning in the light of the specification and prosecution history, and identify corresponding elements disclosed in the allegedly

anticipating reference." Lindemann, 730 F.2d at 1458, 221 USPQ at 485; Kalman, 713 F.2d at 771, 218 USPQ at 789.

"The test for determining if a reference anticipates a claim of a patent is whether the reference contains within its four corners adequate directions for the practice of the patent claim ... ." Kistler Instrument A.G. v. United States, 628 F.2d 1303, 1311, 203 USPQ 511, 519, aff'd., 211 USPQ 920 (Ct. Cl. 1980). The reference, whether foreign or domestic, patent or otherwise, must be construed strictly for what it "clearly and definitely discloses." Application of Boling, 292 F.2d 306, 310-11, 130 USPQ 161, 164 (CCPA 1961); Aluminum Co. of Am. v. Sperry Products, Inc., 285 F.2d 911, 922, 127 USPQ 394, 403 (6th Cir. 1960), cert. denied, 368 U.S. 890 (1961). A patent is not anticipated by a reference "unless the latter exhibits the invention in such full, clear and exact terms as to enable any person skilled in the art to practice it without making experiments." 285 F.2d at 922, 127 USPQ at 403.

Independent claims 7 and 18 both provide, *inter alia*, an extravasation detection device comprising at least a first energy source that is adapted to supply X-ray energy or gamma ray energy to tissue in the vicinity of a site along a path of potential extravasation of fluid from a blood vessel into which fluid is injected. The extravasation detection device further comprises at least a first sensor to measure a signal resulting from the energy supplied to the tissue by the first energy source. The signal is proportional to the X-ray energy or gamma ray energy transformed, reflected, scattered or absorbed by an extravasated fluid present in the vicinity of the site. The extravasation detection device also comprises an indicator to provide an indication of the occurrence of extravasation.

To the contrary, sensor 140 of Uber III is designed to sense contrast concentration within a body of a patient to provide feedback to a control system to control injection of contrast into the patient. In one embodiment for use with computed tomography (CT) contrast, sensor 140 of Uber III includes a source of radioactive material 144 and a radiation detector 142. Unlike the present invention, Uber III does not even address the detection of extravasation. In that regard, there is no disclosure or suggestion in Uber III to provide a first energy source adapted to supply X-ray energy or gamma ray energy to

tissue in the vicinity of a site along a path of potential extravasation of fluid from a blood vessel into which fluid is injected. Likewise, there is no disclosure or suggestion in Uber III of an indicator to provide an indication of the occurrence of extravasation. Under the appropriate standard, as set forth above, Uber III does not and cannot anticipate the present invention.

The Examiner also rejected Claims 11, 35 and 36 under 35 U.S.C. 102(b) "as being anticipated by Mine or Monaghan." Specifically, the Examiner asserted that:

> Mine and Monaghan each disclose an ultrasound source and sensor. The sensor is capable of measuring a signal that inherently is proportional to ultrasound energy reflected by a fluid/contrast agent in the vicinity of the site. The source and sensor do not directly contact the skin.

Applicants respectfully traversed the Examiner's rejection

Mine discloses an ultrasound imaging and diagnostic ultrasound system which can be used in connection with an ultrasound contrast medium including bubbles which reflect and scatter ultrasonic energy. The system of Mine adopts a contrast echo technique to detect sound harmonics resulting from nonlinear scattering of bubbles of the contrast medium to display an image of the distribution of the bubbles two-dimensionally, and to perform measurement utilizing the Doppler effect. See, for example, col 4, line 62 to col. 5, line 2. In the imaging system of Mine, ultrasound energy is transmitted to a diagnostic region such as the cardiac muscle wherein it is reflected and scattered, exhibiting non-linear characteristics which cause harmonics. Resulting ultrasound echoes contain a component emanating from living tissue except the contrast medium (bubbles) and components emanating from the contrast medium. Transducers receive the echoes and convert the echoes into electrical signals from which an image is produced. See Col. 9, lines 29 -67. Unlike the present invention, Mine does not even address the problem of detecting extravasation of a fluid from a blood vessel into which fluid is injected.

Contrary to the disclosure of Mine, independent claim 11 of the present invention, as amended, sets forth an apparatus for the detection of extravasation including at least a first energy source adapted to supply ultrasonic energy to tissue in the vicinity of a site

along a path of potential extravasation of fluid from a blood vessel into which fluid is injected. Further, the apparatus of claim 11 also includes at least a first sensor to measure a signal resulting from the energy supplied to the tissue and an indicator to provide an indication of the occurrence of extravasation. Mine does not disclose or suggest a first energy source adapted to supply ultrasonic energy to tissue in the vicinity of a site along path of potential extravasation of fluid from a blood vessel into which fluid is injected. Furthermore, Mine does not disclose or suggest an indicator to provide an indication of the occurrence of extravasation.

Like Mine, Monaghan discloses an ultrasonic imaging system. Also like Mine, Monaghan does not even address the problem of detecting extravasation from a blood vessel into which fluid is injected.

Like Mine, Monaghan does not disclose or suggest a first energy source adapted to supply ultrasonic energy to tissue in the vicinity of a site along path of potential extravasation of fluid from a blood vessel into which fluid is injected. Further like Mine, Monaghan does not disclose or suggest an indicator to provide an indication of the occurrence of extravasation.

The Examiner further rejected Claims 9, 10, 16-21, 23, 24, 27, 31, 32, and 39-41 under 35 U.S.C. 103(a) "as being unpatentable over Uber III et al ('026) in view of Atkins." Specifically, the Examiner asserted that:

> Uber III et al disclose an x-ray imaging device and a means for detecting radioactive radiation that is sensitive to the amount of contrast agent in a body portion. Uber et al further disclose the use of a power injector for injecting the contrast agent into the patient. Uber Ill et al disclose monitoring the contrast agent levels in a patient's tissues (see figure 6 for example). Uber III et al does not specifically disclose that the monitoring of the contrast agent is used to detect extravasation, however, Uber III et al disclose that the automated injector control improves the efficiency of the system and exposes the patient to a reduced amount of contrast agent. Atkins discloses a device that detects the presence of extravasation of an injected contrast medium and provides a feedback to an electronically controlled injector. Atkins discloses measuring a baseline signal and comparing a measured signal after the injection to the baseline to determine if extravasation has occurred. Extravasation is well known to

> be harmful to the patient. Therefore, it would have been obvious to one skilled in the art to have modified Uber Ill et al such that the detected amounts of contrast agent can be used to monitor the presence of extravasation and the injector is thus controlled based upon these amounts in order to reduce the effects of such contrast agent leakage on the patient.

Applicants respectfully traverse the Examiner's rejection.

As described above, sensor 140 of Uber III is designed to sense contrast concentration within a body of a patient to provide feedback to a control system to control injection of contrast into the patient. Uber III does not even address the problem of extravasation. Generally, there is no disclosure or suggestion in Uber III to provide a first energy source adapted to supply X-ray energy, gamma ray energy, ultrasonic energy or any other type of energy to tissue in the vicinity of a site along a path of potential extravasation of fluid from a blood vessel into which fluid is injected or in the vicinity of a fluid injection site. Likewise, there is no disclosure or suggestion in Uber III of an indicator to provide an indication of the occurrence of extravasation. There is also no disclosure or suggestion in Uber III of analyzing a measured signal resulting form supplying X-ray, gamma ray or ultrasonic energy along a path of potential extravasation to determine whether an extravasated fluid is present in the vicinity of the site. Further, there is no disclosure or suggestion in Uber III of an injector system including an extravasation system in which X-ray energy, gamma ray energy or ultrasonic energy is supplied to a fluid injection site wherein an injection procedure is terminated when an extravasated fluid is detected by the extravasation detection system.

Moreover, contrary to the Examiner's assertion, one cannot combine the disclosure of Atkins with that of Uber III to arrive at the present invention. In that regard, Atkins discloses a photo-plethysmographic sensor which measures the optical scattering properties of capillary blood to detect the presence of extravasated fluids in tissue. Because light is heavily absorbed in tissue, however, the sensitivity of photo-plethysmographs is generally limited to the top ¼ inch of tissue. Many extravasations, however, occur deeper than ¼ inch. Moreover, the injection medium may flow into interstitial spaces remote from the photo-plethysmograph sensors and go undetected. Combining the disclosure of Uber III with that of Atkins would, at most, result in an

X-ray imaging system including a feedback sensor (sensor 140 of Uber III)) to provide feedback of contrast concentration in the body and a photo-plethysmographic extravasation sensor (Atkins) to detect extravasation of injected contrast.

There is no motivation in either Uber III or Atkins modify the disclosures thereof to provide an extravasation detection apparatus, device or method in which X-ray energy or gamma ray energy is transmitted into tissue in the vicinity of a site along a path of potential extravasation or in the vicinity of a fluid injection site. See, for example, *Ex parte* Chicago Rawhide Mfg. Co., 223 USPQ 351, 353 (P.O. Bd. Appl. 1984) ("The prior art must provide a motivation or reason for a worker in the art without the benefit of appellant's specification to make the necessary changes in the reference device."); Schenk v. Norton, 218 USPQ 698, 702 (Fed. Cir. 1983) ("Modification unwarranted by the disclosure of a reference is improper."); Ex Parte Acosta, 211 USPQ 636, 637 (P.O. Bd. Appls. 1980) (Examiner's combination of two references is improper where there is no basis in the record from which it can reasonably be inferred that one skilled in the art would have been led or motivated to modify the primary reference in the manner proposed by the Examiner.).

The Examiner is correct that extravasation is a well known problem that can be quite harmful to patients. However, even though the problem of extravasation has existed for many years, prior to the present invention (to the knowledge of the Applicants), it has never been conceived to apply X-ray energy, gamma ray energy or ultrasonic energy to tissue along a path of potential extravasation of injected fluid to detect extravasation. The devices, systems and methods of the present invention are, for example, particularly useful in detection of contrast medium (for example, a CT contrast medium) that is designed to enhance images in procedures in which the imaging energy is X-ray energy or gamma ray energy (for example, CT imaging procedures). Unlike photo-plethysmographic extravasation sensors such as disclosed in Atkins and other types of extravasation sensors, the extravasation detection devices and methods of the present invention, in which X-ray energy or gamma ray energy is transmitted into tissue along the path of potential extravasation, are sensitive to extravasation, even at depths

beyond the top layers of tissue and in interstitial spaces remote from the detection apparatus.

Given the lack of disclosure in Uber III and/or Atkins to use X-ray energy in the detection of extravasation and the lack of motivation therein to, first, combine the disclosures thereof and, subsequently, to modify the disclosures thereof in a manner to arrive at the present invention, Applicants respectfully assert that the Examiner is impermissibly using the disclosure of the present invention as a guide in modifying the teachings of Uber III and/or Atkins in an attempt to reconstruct the present invention. As the Federal Circuit stated in Orthopedic Equipment Co. , Inc. v. United States, 702 F. 2d 1005, 1012, 217 USPQ 193, 199 (Fed. Cir. 1983):

> It is wrong to use the patent in suit as a guide through the maze of prior art references, combining the right references in the right way so as to achieve the result of the claims in suit. Monday morning quarterbacking is quite improper when resolving the question of nonobviousness in a court of law.

The Examiner also rejected claims 12 and 13 under 35 U.S.C. 103(a) "as being unpatentable over Mine or Monaghan in view of Atkins." Specifically, the Examiner asserted that:

> Mine and Monaghan each disclose an ultrasound source and sensor. The sensor is capable of measuring a signal that inherently is proportional to ultrasound energy reflected by a fluid/contrast agent in the vicinity of the site. Atkins discloses a device that detects the presence of extravasation of an injected contrast medium and provides a feedback to an electronically controlled injector. Atkins discloses measuring a baseline signal and comparing a measured signal after the injection to the baseline to determine if extravasation has occurred. Extravasation is well known to be harmful to the patient. Therefore, it would have been obvious to one skilled in the art to have modified Mine or Monaghan such that the detected amounts of contrast agent can be used to monitor the presence of extravasation and the injector is thus controlled based upon these amounts in order to reduce the effects of such contrast agent leakage on the patient.

For the reasons set forth above and other reasons, Applicants respectfully traverse the Examiner's rejection. Atkins does not overcome the deficiencies of Mine and/or Monaghan set forth above.

As discussed above, each of Mine and Monaghan disclose an ultrasound imaging device. Neither Mine nor Monaghan even address the problem of extravasation. Combination of the disclosures of Mine and/or Monaghan with the disclosure of Atkins would result, at most, in an ultrasound imaging system in which a photo-plethysmographic extravasation sensor (Atkins) is used to detect extravasation.

Once again, the Examiner is correct that extravasation is a well known problem that can be quite harmful to patients. However, even though the problem of extravasation has existed form many years, prior to the present invention (to the knowledge of the present inventors), it has never been conceived to apply X-ray energy, gamma ray energy or ultrasound energy to tissue along a path of potential extravasation to detect extravasation. The devices, systems and methods of the present invention are, for example, particularly useful in detection of extravasation of contrast medium that is designed to enhance images in imaging procedures in which the imaging energy is ultrasonic energy. Unlike photo-plethysmographic extravasation sensors such as disclosed in Atkins and other types of extravasation sensors, the extravasation detection devices and methods of the present invention, in which ultrasound energy is transmitted into tissue along the path of potential extravasation, are sensitive to extravasation, even at depths beyond the top layers of tissue and in interstitial spaces remote from the detection apparatus. Once again, the Examiner cannot use the present specification as a guide as a guide in modifying the teachings of Mine, Monaghan and/or Atkins in an attempt to reconstruct the present invention.

The Examiner also rejected Claims 22, and 28-30 under 35 U.S.C. 103(a) as being "unpatentable over Unger et al ('438) in view of Atkins." Specifically, the Examiner asserted that:

> Unger et al discloses an MR imaging device and a means for detecting a signal that is sensitive to the amount of contrast agent in a body portion. Unger et al disclose mixing an additive with a contrast agent and injecting the mixture into a patient. The additive affects the measured signal. Atkins discloses a device that detects the presence of extravasation of an injected contrast medium. Atkins discloses measuring a baseline signal and comparing a measured signal after the injection to the baseline to determine if extravasation has occurred. Extravasation is well known to

> be harmful to the patient. Therefore, it would have been obvious to one skilled in the art to have modified Unger et al such that the detected amounts of contrast agent can be used to monitor the presence of extravasation in order to reduce the effects of such contrast agent leakage on the patient.

Unger discloses lipids as additives to magnetic resonance (MR) contrast agents, which has particularly benefit in magnetic resonance imaging (MRI) of the liver, blood pool and reticuloendothelial system. Unger does not even address the problem of extravasation of fluid from a blood vessel into which the fluid is injected. As described above, Atkins disclosed a photo-plethysmographic extravasation sensor. Combining the disclosure of Unger with that of Atkins would result, at most, in an MR imaging procedure in which the contrast medium of Unger is injected and in which a photo-plethysmographic extravasation sensor as disclosed in Atkins is used to detect extravasation.

Applicants have amended claims 22 to indicate that a signal resulting from the energy supplied to the tissue is measured to determine if extravasation has occurred, wherein the energy is of a different type than imaging energy adapted to be used in connection with the contrast medium. The additive affects the signal resulting from the application of the energy. The is no disclosure or suggestion in the disclosure of Unger and/or Atkins to add an additive to a contrast medium that affects a signal resulting from application of energy other than the imaging energy to tissue.

In view of the above amendments and remarks, Applicants respectfully request that the Examiner withdraw the rejections of the claims, indicate the allowability of the claims and arrange for an official Notice of Allowance to be issued in due course.

Respectfully submitted,

Henry E. Bartony Jr.

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Henry E. Bartony, Jr.
Reg. No. 34,772

Medrad, Inc.
One Medrad Drive
Indianola, PA 15051
Telephone: (412) 767-2400 x3019